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COMPARATIVE INVESTIGATION OF THE PHAGOCYTIC REACTION TO FOREIGN PROTEINS AND TO TOXICOINFECTIOUS INFLUENCES IN ANIMALS WITH DIFFERENT TYPES OF NERVOUS SYSTEM

(Dogs and White Rats)

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COMPARATIVE INVESTIGATION OF THE PHAGOCYTIC REACTION TO FOREIGN PROTEINS AND TO TOXICOINFECTIOUS INFLUENCES IN ANIMALS WITH DIFFERENT TYPES OF NERVOUS SYSTEM

(Dogs and White Rats)

[Following is a translation of an article by L. I. Kryachko in Patolog. Fiziol. i Eksper. Terapiya (Pathological Physiology and Experimental Therapy), Vol. IV, No. 1, 1960, pages 53-58.]

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The problem of evaluating the reactivity of the body by means of various immunological tests, worked out in his time in the school of A. A. Bogomolets, is closely associated with the study of the constitutional characteristics of the organism being investigated. One of the means of investigating this problem is the study of the relationship of the reactivity and the tests characterizing it to the type of nervous system of the animals. The bibliography devoted to this question is sparse and contradictory. A number of authors (2-7) have found this relationship; others (1) have not.

The task of the present work was the study of the characteristics of the protective reactivity of animals with different types of nervous systems by means of a comparative investigation of the reactions of cellular immunity to a foreign protein of non-microbial origin and to a toxico-infectious influence in the same animals. Here, the first procedure was regarded as a test showing the

potential capacity of the phagocytic reaction, which, as is well known, plays an important protective part in the infectious process.

The investigation was carried out on 14 white rats having typological nervous system characteristics demonstrated according to the L. I. Kotlyarevskiy method and on four dogs, obtained from G. Ya. Cuobis, in which the nervous system types had been determined. Among the white rats three animals were of the strong well-balanced type; six, of the markedly excitable type; two, of the weak inhibitory type; and three, of intermediate type.

The typological characteristics of the nervous system of the dogs were characterized in the following way: 1) Seryy, male, weight 25 kg, strong, mobile, unrestrained; 2) Pirat, male, weight 21 kg., strong, mobile, with slight predominance of excitation; 3) Kuchum, male, weight 22 kg. weak, inert, inhibitory; 4) Malyuk, male, weight 17 kg; an animal of the strong unbalanced type. However, as the result of work associated with prolonged overstrain of cortical activity a marked weakening of the stimulatory process was observed in this dog, and it may be regarded as an animals with a weakened functional condition of the cerebral cortex.

All the animals were given intramuscular injections of foreign protein (placental gamma-globulin for measles prophylaxis): white rats in a dose of 0.5 cc for each animal; dogs, in a dose of 0.14 cubic centimeter/ kilogram. Then, after two months, the white rats were infected by means of the intraperitoneal administration of 4,500,000,000 microbial bodies of the adapted hemolytic streptococcus, and the dogs were given a staphylococcal toxin in a dose of 0.5 cubic centimeter per kilogram subcutaneously.

Changes in the phagocytic reaction in response to the injection of gamma-globulin were compared with the changes of this reaction during the streptococcal infection and the staphylococcal intoxication.

The following method was used for investigating the phagocytic reaction. Blood samples taken from the ears of the dogs and from the tails of the rats were mixed with five-percent sodium citrate in volumes of 0.1 cubic centimeter of blood for 0.05 cubic centimeter of citrate, and 0.05 cubic centimeter of a suspension of 2,000,000,000 organisms of a 24-hour bouillon culture of washed hemolytic streptococcus xxxxxx in physiological solution was added to the mixture. After mixing x by means of shaking the mixture was put into an incubator for 30 minutes (at 38°), smears were made which were fixed in methyl alcohol and stained by the Romanowsky-Giemsa method. In counting 100 neutrophils the percentage of phagocytizing leucocytes and the average number of microbes phagocytized by a x single leucocyte (phagocytic index) were recorded. We investigated the phagocytosis for three days, during which time the effect of the gamma-globulin on the phagocytic reactions of the dogs was most pronounced (afterwards, the phagocytic index /returned usually to the original level). In the staphylococcal intoxication the phagocytic reaction was investigated for 15-20 days. In white rats the phagocytic reaction was investigated 14 days both after the injection of gamma-globulin and during the streptococcal infection.

In Figs. 1 and 2 the changes in the phagocytic reaction of dogs xxxxx with different types of nervous systems are presented graphically after the injection of gamma-globulin and during the staphylococcal intoxication.

As is seen from Fig. 1, in the dogs of the strong type, Seryy and Pirat, an hour after the injection of gamma-globulin a considerable activation of the phagocytic reaction was observed. Similar changes in phagocytosis were noted in these dogs also after the injection of the staphylococcal toxin. It may be seen that the configuration of the phagocytic curve was the same for the two types of effect presented.

From Fig. 2 it is seen that in the dog /of the weak type, Kuchum, and in the dog Malysh, the animal with the weakened functional condition of the cerebral cortex,

a marked inhibition of the phagocytic reaction was observed during intoxication, just as in response to the injection of gamma-globulin, even in the first few hours after the injection of these preparations. Then, in Kuchum for seven days after the intoxication and in Malysh throughout the entire investigation (15 days) an exceptionally low degree of phagocytic activity was noted, whereas the phagocytic index in the dogs of the strong type was high. It should be noted that the clinical course of the disease was in complete accordance with the nature of the phagocytic reaction in all animals.

Because the staphylococcal toxin possesses a dermato-necrotic effect an extensive area of skin necrosis, the surface of which x was infected, was formed on the fifth to seventh day in all dogs at the site of injection of the toxin.

After the microscopic examination of the smears--impressions taken from the surface of the necrotic area--we became convinced of the distinct difference between the microflora found in them. Here, a the degree of infection of the necrotic area corresponded to the intensity of the phagocytic reaction. In the dogs of the strong type, Serzy and Pirat, mixed ordinary flora was found, chiefly staphylococci; In the dogs Kuchum and Malysh, an almost pure culture of streptococci. Then, in Kuchum on the 10th day the increase in the phagocytic activity of the leucocytes mem coincided with the onset of clearing of the necrotic area. In Malysh, against the background of an exceptionally low phagocytic reaction, the surface of the area of necrosis increased in size, involved the sexual organs; an ascending pyelonephritis developed, and the animal died from streptococcal septicemia.

Therefore, the reaction of cellular immunity depends, on the one hand, on the type of nervous system of the dogs. The animal of the strong type with a weakened functional state of the cerebral cortex reacted in the same way as dogs of the weak type. On the other hand, the changes in the phagocytic reactions after these two types of effect (injection of gamma-globulin and staphylococcal toxin) were similar. Let us

compare the data described above with the changes in the phagocytic reaction of the white rats.

In Fig. 3 comparative data are presented of the change in the phagocytic reaction in two white rats of the strong type. In these animals, even an hour after the injection of the gamma-globulin, a distinct activation of phagocytosis was observed. The same changes were noted in the first few hours after infection with the streptococcus, which corresponded with the favorable course of the disease.

From Fig. 4 it is seen that in two white rats of the weak type similar changes in the phagocytic reaction (marked inhibition of phagocytosis after either effect were observed after the injection of gamma-globulin and during the streptococcal infection.

In rat No 4 the low degree of phagocytic activity of the leucocytes noted throughout the entire disease corresponded to the severe clinical course of the infection with prolonged bacteriemia. Rat No 8 died from a fulminant streptococcal septicemia against the background of a weakening of phagocytosis. Similar relationships were observed in the other white rats.

Therefore, comparison of the phagocytic reaction in the same animals to the injection of gamma-globulin with the nature of phagocytosis during a staphylococcal intoxication or streptococcal infection as well as with the clinical course of the disease showed the following: 1) the similar nature of changes in the phagocytic reaction after these influences; 2) the most favorable course of the disease in those animals in which the gamma-globulin produced a stimulation of phagocytosis.

In the animals in which the effect of stimulation was insignificant or the phagocytic reaction was inhibited the most severe course of the toxicoinfectious process was noted up to a lethal outcome. Inhibition of the phagocytic reaction which we found in animals of the weak type or with a weakened functional state of the cerebral cortex produced by doses of gamma-globulin which

exerted a stimulating effect on animals of the strong type was apparently the result of the ultraboundary effect. Naturally, the injection of protein of microbial origin, which is much stronger stimulus than gamma-globulin, produced an even more profound ultraboundary effect in the immune system of these animals with a corresponding influence on the clinical course of the diseases.

The coincidence of the phagocytic reactions to foreign protein of microbial and non-microbial origin in the same individuals leads to the idea of the possibility of using the phagocytic reaction as a prognostic test, under conditions of immunological stimulation, of the change in this reaction during the subsequent infectious disease. This would make it possible to demonstrate the reactivity level normally before infection and, to a certain degree, to predict the course and outcome of the disease.

Conclusions

1. Doses of protein preparations which stimulate the phagocytic reaction in animals with the strong type of nervous system exert a depressive effect in animals with the weak type of nervous system.

2. The most favorable course of a toxicoinfectious disease was observed in animals which showed a considerable stimulation of phagocytosis after the injection of gamma-globulin.

3. The coincidence of the nature of the phagocytic reaction to gamma-globulin and the toxicoinfectious influence in the same animals attests to the possibility of using a gamma-globulin injection as a prognostic test for demonstrating the reactivity level of the given animal.

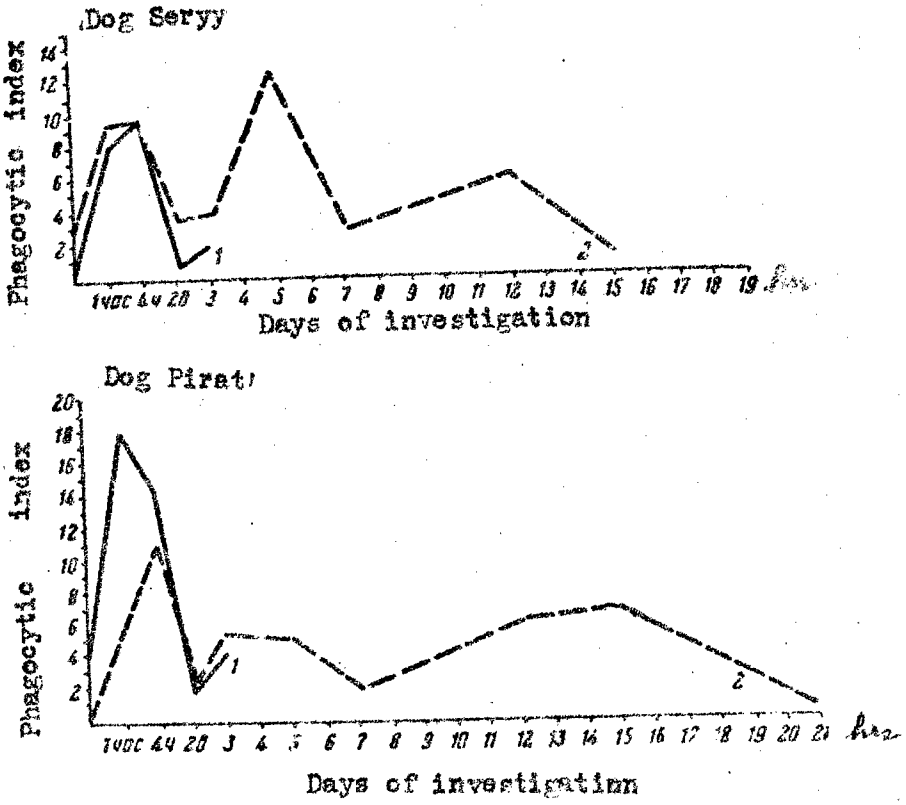

Fig. 1. Comparative data of change in phagocytic index in dogs with the strong type of nervous system.

1) changes in phagocytic index after injection of gamma-globulin;

2) changes in phagocytic index during staphylococcal intoxication.

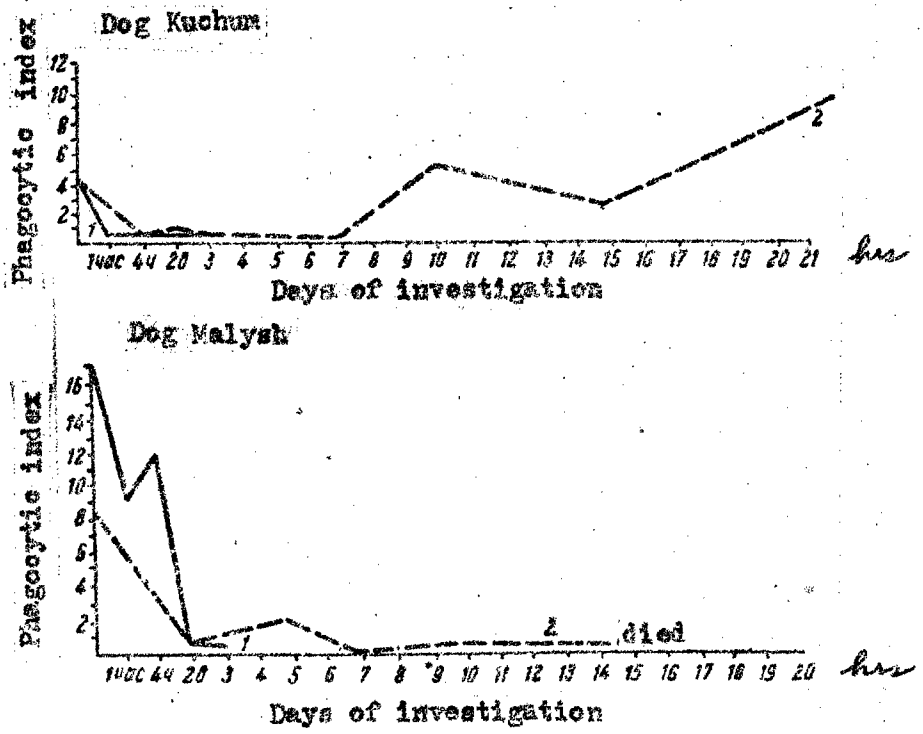

Fig. 2. Comparative data of change in phagocytic index in dog Kuchum of the weak type, and in dog Malysh with weakened functional state of the cerebral cortex. The key is the same as for Fig. 1.

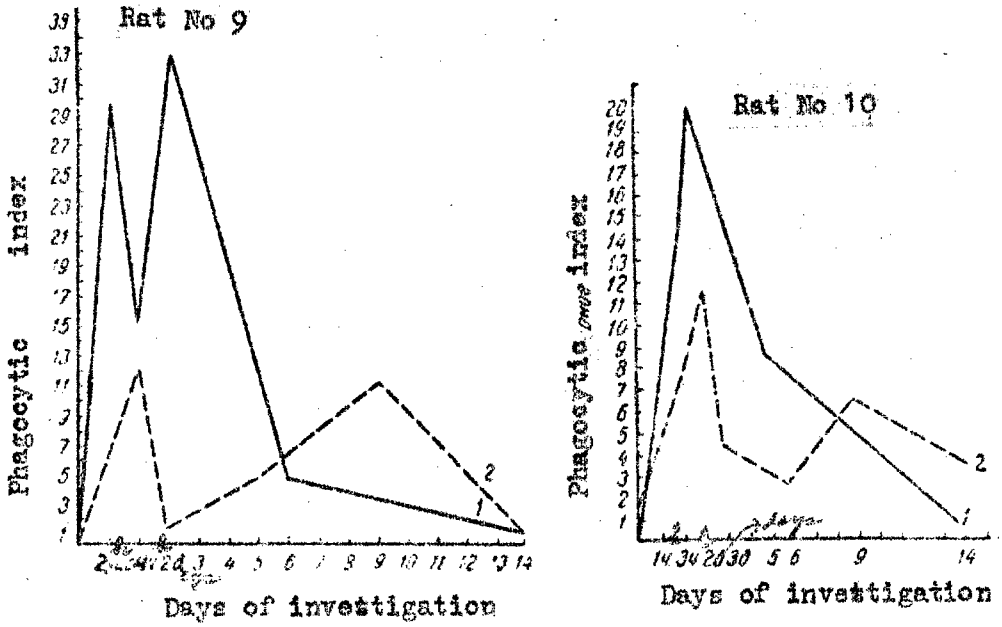

Fig. 3. Comparative data of the change in phagocytic index of rats with the strong type of nervous system.

1) changes in phagocytic index after injection of gamma-globulin;

2) changes in phagocytic index during streptococcocal infection.

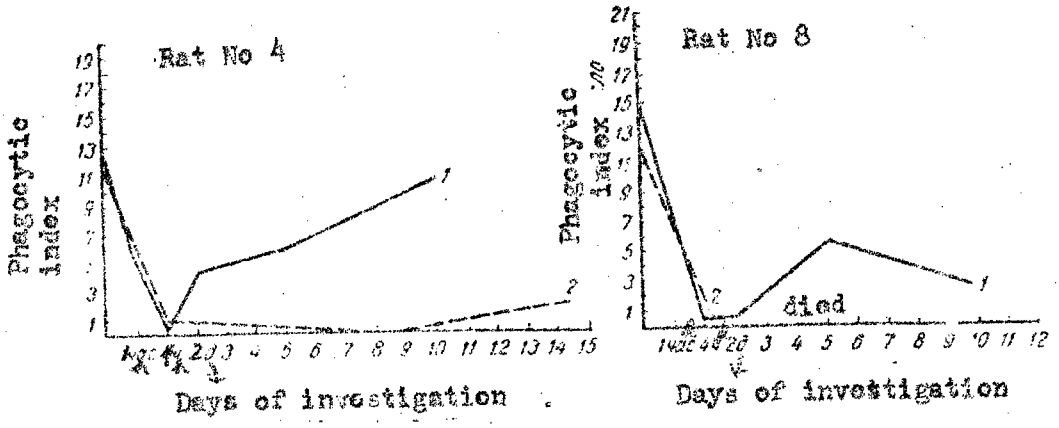

Fig. 4. Comparative data of change in phagocytic reaction in rats with the weak type of nervous system.

The key is the same as for Fig. 3.

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